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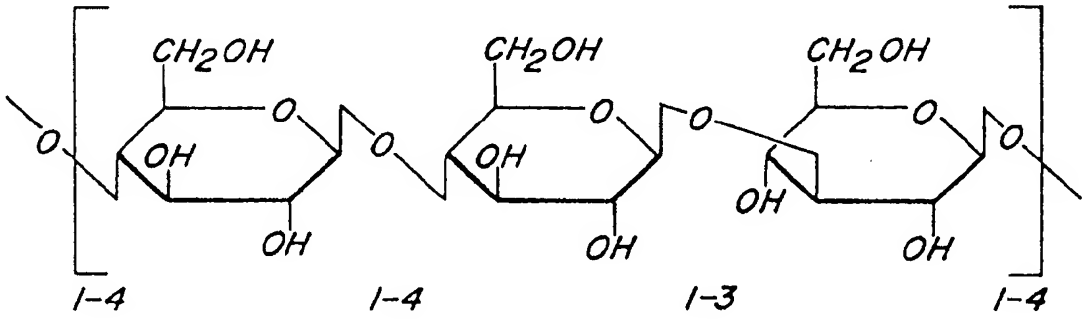

(57) Abstract

A topical composition for healing treatment of burns and wounds and scarring therefrom has as the active ingredient cereal–derived (1–3) (1–4) β–D–glucan at about 0.5–15 w/w percent. The composition may be formulated in various forms with creams and gels being preferred for application to the skin.

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PCT PATENT APPLICATION

β-D-GLUCAN TOPICAL COMPOSITION

BACKGROUND OF THE INVENTION

Field of the Invention: This invention relates generally to topical compositions for the treatment of superficial and partial thickness burns and wounds of the skin and mucosa. More particularly, the invention pertains to formulations of topical creams and gels providing cleansing, moisturizing, soothing and anti-pruritic activity for topical therapeutic treatment of wounds and burns and other skin loss injuries and conditions.

State of the Art:

A group of complex polysaccharides known as glucans are found in the cell walls of yeast and bacteria. Though the structures of the microbial-derived glucans have not been completely elucidated, they are known to include long-chain carbohydrate polymers composed solely of β-D-glucan residues with 1,3 linkages or a combination of 1,3- and 1,6-linkages. In the cell walls of the yeast *Saccharomyces cerevisiae*, the glucans may also be associated with mannan, another complex polysaccharide.

Studies have indicated that yeast-derived 1,3-glucan activates macrophages, including phages with immunological activity against tumor growth. The 1,6-glucans were found to be inactive relative to macrophages. Such is reported by Di Luzio et al. in THE MACROPHAGE IN NEOPLASIA, Mary A. Fink, editor, 1976, Academic Press, New York, pp 181-182.

In U.S. Patent No. 5,158,772 of Davis, the incorporation of a microbial-derived beta-1,3-glucan-type polysaccharide in a topical composition is disclosed. The polysaccharide is produced by a bacterial microorganism known as *Cellulomonas flavigena*. The functions of the polysaccharide in the topical

composition are described as three-fold, i.e. (a) its effectiveness as a water-holding agent by which it controls the fluidity, appearance and "feel" of a composition, (b) its viscosity raising effect, and (c) its ability to suspend other cosmetic and therapeutic agents such as dyes, drugs, germicides, anesthetics, etc. as a carrier.

In a U.S. Patent Application of Williams and Lawin, bearing S.N. 08/423,838 and commonly assigned with this application, a mesh matrix wound dressing is disclosed which incorporates cereal-derived β-D-glucan and collagen in a cast burn dressing.

A topical healing unguent is needed for treatment of burns and wounds of the skin and mucosa where a wound dressing is not indicated.

SUMMARY OF THE INVENTION

The invention comprises a multi-purpose topical composition for application to the skin and mucosa. It is intended for use as a topically applied cream or gel to provide cleansing and soothing relief of superficial and partial thickness burns, as a moisturizer to enhance water retention of the stratum corneum, and to relieve the itching associated with hypertrophic or keloid scarring.

The active ingredient of the topical composition of the invention is being investigated as a possible biological response modifier and macrophage stimulant.

The primary active component of the topical composition is cereal-derived β-D-Glucan, chemically comprising a large number of glucopyranosyl units determined to be linked by (1-3) and (1-4) linkages. The preferred active agent is β-D-Glucan derived from oats, although the glucans from barley, wheat and/or other cereal grains may be used for the topical composition, provided the (1-4) (1-3) β-D-Glucan can be extracted economically.

As generally formulated, the composition of the topical cream of the invention comprises the following, where the indicated concentration of each component is uniformly given as a percentage of the total of all components:

cereal-derived β-D-Glucan (active agent)	about 0.5-15 w/w %
ointment base	about 10-20 w/w %
humectant(s)	about 2-6 w/w %
suspending/viscosity increasing agent(s)	about 0.01-8.0 w/w %
stiffening agent(s)	about 0.5-6 w/w %
emulsifying/solubilizing agent(s)	about 0.1-8 w/w %
antimicrobial agent(s)	about 0.1-2 w/w %
plasticizer(s)	about 5-15 w/w %
solvent(s)	balance

Some ingredients may have several functions. For example, glycerol may serve both as a solvent and a plasticizer, and propylene glycol may serve as a solvent, humectant and plasticizer.

A general formulation for a gel composition of the invention is:

cereal derived β-D-Glucan (active agent)	about 0.5-15w/w %
water	about 80-98 w/w %
suspending/viscosity increasing agent(s)	about 0.5-8 w/w %
emulsifying/solubilizing agent(s)	about 0-5 w/w %
antimicrobial agent(s)	about 0.05-1 w/w %

The cereal-derived β-D-Glucan in this composition is significantly different from glucans obtained from other sources, including β-D-Glucans derived from yeast such as *Saccharomyces cerevisiae* and bacteria such as *Cellulomonas flavigena*.

The primary source of β-Glucan has historically been yeast and bacterial cells. However, the cereal-derived (1-4)(1-3) β-D-glucan useful in the invention is distinctive from microbial-derived glucans which have all (1-3) linkages or primarily (1-3) linkages with a few (1-6) linkages. The molecular weight of the mixed-linkage cereal-derived β-D-Glucan used in this invention is much greater than that of the microbial-derived glucans.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a drawing of a generalized chemical structure of microbe-derived (1-3) β-D-glucan used in a prior art composition;

FIG. 2 is a drawing of a generalized chemical structure of microbe-derived (1-3)(1-6) β-D-glucan; and

FIG. 3 is a drawing of a proposed generalized chemical structure of mixed-linkage cereal-derived (1-3)(1-4) β-D-glucan used in a topical composition of the invention.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the invention, new compositions for multi-purpose topical treatment are presented wherein the active ingredient is a cereal-derived β-D-glucan, identified herein as "CDG". The invention pertains to various topical compositions including a solvent base varying from essentially all water to essentially all oil. The invention includes topical compositions variously known as unguents, creams, gels, emollients, lotions and oils, each with a generally characteristic solvent composition, and having a form ranging from liquid to semisolid.

Compounds classified as β-glucans comprise a large group of high molecular weight polymers containing glucopyranosyl units in β-linked chains. β-glucans are found in essentially all living cells which are enclosed by cell walls, with considerable structural variation dependent on source. They are highly unbranched homopolysaccharides and isomerically

diaposed to alpha-D-glucan (e.g. starch) which is typically non-functional as a structural support component of the cell.

As depicted in FIG. 1, glucans derived from microbes have been generally characterized as essentially comprising (1-3) - linked chains of glucopyranosyl units. With the recent advances in test identification methods, yeast-derived glucans having primarily (1-3)-linkages with a relatively small number of (1-6)-linkages (FIG. 2) have been identified. Yeast-derived glucan polymers are often associated with mannose, and typically have a helically coiled chain shape.

The mixed linkage glucan polymers found in cereals are quite different from yeast-derived and bacteria-derived polymers. Glucans derived from cereal grains, as shown in FIG. 3, have (1-3) and (1-4) linkages and generally have a linear or kinked linear chain.

Cereal-derived glucan (CDG) may be characterized as follows:

a. CDG is a long chain, unbranched polysaccharide which typically comprises about 3-4 percent of oat and barley grains. The CDG concentration is greater, e.g. 7-10 percent, in the milled bran fraction of oats.

b. CDG is found in the endosperm and aleurone cell walls of most cereal grains. The microbe-derived glucans occur in the cell wall of the yeast or bacteria.

c. CDG is a mixed-linkage molecule containing about 70 percent (1-4)-linkages and about 30 percent (1-3)-linkages. The (1-3)-linked units mostly occur singly whereas the (1-4)-linked units typically occur in groups of three or four glucopyranosyl units. Thus, the resultant structure is a series of short runs of 3 or 4 (1-4)-linked glucopyranosyl units, adjacent runs connected by (1-3) linkages. The frequencies of the groups of three (cellotriosyl) and four (cellotetraosyl) glucopyranosyl units also tend to be characteristic of the source, being affected by cereal variety, tissue age, and stage of maturity. Oat-derived CDG typically has more of the groups of three consecutive (1-4)-linked glucopyranosyl units than does barley-derived CDG. The

ratio of trisaccharide to tetrasaccharide groups is about 2:1 for oats and closer to 3:1 for barley. CDG differs from microbe-derived glucans, which have all (1-3)-linkages or mostly (1-3)-linkages with some (1-6)-linkages.

d. CDG is a linear molecule, while yeast-derived glucan forms a helical shape.

e. The degree of polymerization of CDG is in the range of about 1200-1800. On the other hand, yeast-derived β-D-glucan has a much lower degree of polymerization, i.e. about 60-80. Cellulose, the primary constituent of plant cell walls, has all β (1-4) linkages and a degree of polymerization of about 10,000 to 15,000.

f. CDG forms viscous solutions in warm water. On the other hand, yeast-derived glucan is insoluble in water but dispersible in aqueous systems.

g. CDG occurs within the grain with a fairly broad range of MW, i.e. about 200,000 to 700,000. The molecular weight is believed to be dependent upon the grain species, grain source, glucan extraction conditions and particular laboratory. Microbe-derived glucan has a much lower molecular weight, in the range of about 10,000 to 14,000. Cellulose has a molecular weight of about 700,000.

h. The use of CDG as a food component has been studied extensively by various researchers; studies have included the use of CDG in regulation of glucose metabolism, hypoglycemic response, reduction in serum cholesterol, and the like.

Thus, in terms of chemical structure and molecular weight, CDG is much more like cellulose than are the microbial-derived glucans.

Each of the components of the new composition serves a particular function or functions, and is available in purities conducive to use in the particular applications. Thus, a component may comprise United States Pharmacia (USP), National Formulary (NF), or other purified grade appropriate for topical use on burns and wounds on the skin.

In addition to cereal-derived β-D-glucan, the components of the cream formulation include:

a. an ointment base, preferably white petrolatum. An alternative but somewhat less desirable substance for this purpose is lanolin.

b. a solvent, primarily or entirely water. Additional solvents which may be added at generally lower concentrations include natural oils such as cod liver oil, mineral oil, etc., and glycerol or propylene glycol. The water content of the cream formulation is at least about 50 percent.

c. a plasticizer, preferably glycerol. Propylene glycol or another glycol may also be used as a plasticizer.

d. a humectant, preferably propylene glycol.

e. a suspending or viscosity enhancement agent, such as carrageenan. Other possible exemplary agents include polyvinyl alcohol, xanthan gum, agarose, alginate, guar gum, Carbopol 940™ carbomer (B.F. Goodrich), and carboxymethylcellulose (CMC), as well as mixtures thereof. A variation in the concentration of suspending agents is compensated by varying the water (solvent) concentration.

f. an emulsifying or solubilizing agent or agents. Exemplary agents are sodium lauryl sulfate and triethanolamine. In the preferred formulation, a combination of sodium lauryl sulfate and triethanolamine is used.

g. a stiffening agent, preferably cetyl alcohol (hexadecanoic acid). Paraffin may also be used.

h. an antimicrobial agent, preferably one or more parabens. The paraben may be methylparaben, propylparaben, ethylparaben, butyl paraben, or mixtures thereof. Other possible antimicrobial agents are imidurea, benzoic acid and benzoic alcohol.

A preferred formulation of the cream composition of the invention is:

Cereal-derived β-D-glucan	about 0.5-15 w/w %
Petrolatum (white)	about 0.5-15 w/w %
Glycerol	about 5-15 w/w %
Propylene Glycol	about 2-6 w/w %
Cetyl Alcohol (Hexadecanoic Acid)	about 0.5-6 w/w %
Triethanolamine	about 0.1-5 w/w %
Sodium Lauryl Sulfate	about 0.1-5 w/w %
Parabens	about 0.01-2 w/w %
Carrageenan	about 0.01-1.0 w/w %
Water	balance (at least 50%)

A presently most preferred composition of the topical cream is as follows:

Cereal-derived β-D-glucan	about 2 w/w percent
Petrolatum (white)	about 15 w/w percent
Glycerol	about 10 w/w percent
Propylene Glycol	about 4 w/w percent
Cetyl Alcohol (Hexadecanoic Acid)	about 2 w/w percent
Triethanolamine	about 2 w/w percent
Sodium Lauryl Sulfate	about 1 w/w percent
i-Carrageenan	about 0.3 w/w percent
Methyl Paraben	about 0.2 w/w percent
Propyl Paraben	about 0.2 w/w percent
Xanthan Gum	about 0.15 w/w percent
Water	balance (about 63.15 w/w%)

Another preferred embodiment of the cream composition is as follows:

Cereal-derived β-D-glucan	about 2 w/w percent
Petrolatum (white)	about 15 w/w percent
Glycerol	about 10 w/w percent
Propylene Glycol	about 4 w/w percent
Cetyl Alcohol (Hexadecanoic Acid)	about 2 w/w percent
Triethanolamine	about 2 w/w percent
Sodium Lauryl Sulfate	about 1 w/w percent

Parabens	about 0.25 w/w percent
Carrageenan	about 0.1 w/w percent
Water	balance (about 62.75 w/w%)

EXAMPLE A

A 100 g batch of a topical cream of the invention was prepared having the following ingredients, given as g per 100 g total cream composition:

Water	63.15 g/100g
White Petrolatum, m.p. 38-60°C	15.0 g/100g
Glycerol	10.0 g/100g
Propylene Glycol	4.0 g/100g
Cereal(oat)-derived β-D-glucan	2.0 g/100g
Cetyl Alcohol	2.0 g/100g
Triethanolamine	2.0 g/100g
Lauryl Sulfate	1.0 g/100g
i-Carrageenan	0.3 g/100g
Methylparaben	0.2 g/100g
Propylparaben	0.2 g/100g
Xanthan Gum	0.15 g/100g

A stock solution of 4% β-D-glucan was prepared by dissolving 4.0 g of purified oat-derived β-D-glucan (powder) in 96 ml of distilled water in an autoclave bottle. The solution was stirred vigorously and then autoclaved at 121°C with stirring until the glucan was fully dissolved.

To 50 ml of the stock solution of dissolved β-D-glucan were added the remaining ingredients at the above indicated weights. Additional water was added to bring the components of the mixture to the desired final concentrations. The mixture (at 85-90°C) was liquified with constant stirring until all ingredients were dissolved and the mixture was homogeneous. The solution was then homogenized in a Polytron homogenizer for 45 seconds at a speed setting of 3.

The once-homogenized cream composition was cooled to about 50°C and homogenized a second time at the same speed and time conditions. The cream composition was then

dispensed into individual containers and cooled to room temperature.

When topically applied, the cream composition had a desired tactile soothing, non-greasy feeling with a consistency like that of whipped cream. The cream composition provided very good skin moisturization and emollience.

Alternatively, a fat free, water soluble version of the cream may be provided. In such a composition, the levels of Beta D-glucan and the other water soluble components would be increased, and no petrolatum base would be present. The concentration ranges from the examples given above would remain applicable.

A useful gel composition of the invention, including the active ingredient, cereal-derived β-D-glucan, is as follows:

Cereal-derived β-D-glucan	about 0.5-15 %
Water	about 80-98 %
Polyvinyl alcohol	about 0.5-4 %
Xanthan gum and/or CMC	about 0.5-4 %
Other suspending agent(s)	about 0-4 %
Antimicrobial agent(s)	about 0.1-1 %

Other suspending/viscosity increasing agent(s) which may be added include carrageenan, agarose, alginate, Carbomer 940™ thickener, and guar gum, at concentrations of each additional agent at about 0.01-4 %. The use of xanthan gum and/or CMC is particularly advantageous for producing a clear colorless gel.

In addition, one or more emulsifying/solubilizing agents such as triethanolamine may be added at about 2 percent each.

Furthermore, a chelating agent such as ethylene-diaminetetraacetic acid (EDTA) may be added at about 0.1-0.5 percent, generally as its tetrasodium salt.

Thus, a most preferred embodiment of the gel composition comprises:

Cereal-derived β-D-glucan	about 2.0 w/w %
Polyvinyl alcohol	about 2.0 w/w %
Triethanolamine	about 2.0 w/w %
Carboxymethylcellulose (CMC)	about 2.0 w/w %

Additional suspending agent	about 0-4 w/w %
EDTA	about 0.2 w/w %
Methyl Paraben	about 0.2 w/w %
Propyl Paraben	about 0.2 w/w %
Water (at least 80 %)	balance

A preferred additional suspending agent is Carbopol™ 940 carbomer, added at about 0.5 percent.

EXAMPLE B

A 100 g batch of a gel composition of the invention was prepared having the following ingredients:

Water(distilled)	92.9 g/100g
Cereal(oat)-derived β-D-glucan	2.0 g/100g
Triethanolamine	2.0 g/100g
Carboxymethylcellulose (CMC)	1.0 g/100g
Polyvinyl Alcohol	1.0 g/100g
Carbopol™ 940 carbomer(acrylic acid homopolymer)	0.5 g/100g
Ethylenediaminetetraacetic Acid (EDTA)	0.2 g/100g
Methylparaben	0.2 g/100g
Propylparaben	0.2 g/100g

43.9 g of water (room temperature) was placed in a container and stirred rapidly to produce a vortex at the bottom of the container. The weighed-out carbomer was then sifted into the agitated water until it dissolved completely. The remaining dry ingredients were then added to the container while stirring to achieve a uniform mixture/solution. The appropriate quantity (50.0 g) of the cereal(oat)-derived β-D-glucan stock solution of Example A was added to the container, and the mixture was liquified at 85-90°C with constant stirring until all ingredients were dissolved and the solution homogeneous. The gel composition was allowed to cool to room temperature, and dispensed into individual containers.

The gel composition produced by this method had a soothing feeling with high moisturizing and emollient properties.

An oil-based topical composition containing cereal-derived β-D-glucan may be formulated. In this composition, the solvent of the basic cream or gel formulation is changed to be primarily an oil or mixture of oils. The water content is reduced to compensate for the increased concentrations of oil(s). The other ingredients may remain the same or be varied as desired. In the oil composition, the solvent may comprise, for example, all oil(s), or a mixture of oil and water, where the oil fraction is generally greater than the water fraction.

However, the preferred forms of topical compositions for treatment of burns and wounds are, at this time, the cream and gel formulations.

In a method of the invention for management of burns and wounds, the composition may be topically applied to the area of damaged tissue. The glucan containing cream or gel of the invention provides a soothing emollient, moisturizing, anti-pruritic and biologically-derived dermal protection to assist during the skin's recuperative process.

The treatment comprises:

1. thorough cleansing of the burn area or site of tissue destruction;

2. liberal topical application of the topical composition to the affected area; and

3. repeated application of the composition until healing is complete.

The method is useful for management of scars due to burns, wounds or surgery, and the cream or gel is topically applied to the affected hypertrophic or keloid scar. The topical composition provides a more rapid healing of burns or wounds, moisturizing relief for dryness and skin irritation, and a reduction in pruritus. The active ingredient, cereal-derived β-D-glucan may also be a biological response modifier, i.e. a macrophage stimulator.

WHAT IS CLAIMED IS:

1. A topical composition for application to skin and mucosa for burns and wounds and other skin loss injuries and conditions comprising cereal-derived β-D-glucan as an active ingredient in one of a cream base, gel base and oil base.

2. The topical composition of claim 1, wherein said cereal derived β-D-glucan is derived from one of oats, wheat and barley.

3. The topical composition of claim 1, wherein said cereal derived β-D-glucan is derived from oats.

4. The topical composition of claim 1, wherein said cereal derived β-D-glucan is characterized as (1-3)(1-4) β-D-glucan.

5. The topical composition of claim 1, wherein said cereal derived β-D-glucan comprises about 0.5 to 15 w/w percent of said topical composition.

6. The topical composition of claim 1, wherein said cereal derived β-D-glucan comprises about 2-8 w/w percent of said topical composition.

7. The topical composition of claim 1, wherein said composition is a cream, said composition comprising:
cereal-derived β-D-glucan at about 0.5-15 w/w percent;
a solvent including water at about at least 50 w/w percent of the composition;
an ointment base of at least about 10 w/w percent;
a humectant;
a stiffening agent;
an emulsifying/solubilizing agent;

a suspending/viscosity increasing agent;
an antimicrobial agent; and
a plasticizer.

8. The topical composition of claim 7, wherein said solvent comprises at least 50 w/w percent of said topical composition.

9. The topical composition of claim 7, wherein said solvent includes oil at a concentration of up to about 20 w/w percent of said topical composition.

10. The topical composition of claim 7, wherein said oil comprises one or more of cod liver oil, mineral oil, shark liver oil, and glycerol.

11. The topical composition of claim 7, wherein said ointment base comprises one of white petrolatum and lanolin.

12. The topical composition of claim 7, wherein said humectant comprises propylene glycol.

13. The topical composition of claim 7, wherein said stiffening agent is selected from a group comprising cetyl alcohol and paraffin.

14. The topical composition of claim 7, wherein said emulsifying/solubilizing agent is selected from a group including sodium lauryl sulfate and triethanolamine.

15. The topical composition of claim 7, wherein said suspending/viscosity increasing agent is selected from the group comprising polyvinyl alcohol, agarose, alginate, xanthan gum, guar gum,

carboxymethylcellulose, and Carbopol 940™ carbomer.

16. The topical composition of claim 7, wherein said antimicrobial agent is selected from the group comprising methyl paraben, ethyl paraben, butyl paraben, and propyl paraben.

17. The topical composition of claim 7, wherein said plasticizer is selected from one of glycerol and propylene glycol.

18. A composition of a multi-purpose topical cream, comprising:

water	at least 50 w/w %
white petrolatum	about 10-20 w/w %
glycerol	about 5-20 w/w %
propylene glycol	about 2-6 w/w %
cetyl alcohol (hexadecanoic acid)	about 0.5-6 w/w %
cereal-derived β-D-glucan	about 0.5-15 w/w %
triethanolamine	about 0-5 w/w %
sodium lauryl sulfate	about 0.1-5.0 w/w %
antimicrobial agent	about 0.1-2 w/w %, and
i-agarose	about 0.01-0.5 w/w %.

19. The composition of claim 18, further comprising xanthan gum at about 0.1-4.0 %.

20. The composition of claim 18, wherein said antimicrobial agent is selected from the group of parabens including methyl paraben, ethyl paraben, butyl paraben and propyl paraben.

21. A composition of a topical cream for treatment of burns and wounds, comprising:

white petrolatum	about 15 w/w %
glycerol	about 10 w/w %

propylene glycol	about 4 w/w %
cetyl alcohol (hexadecanoid acid)	about 2 w/w %
cereal derived β-D-glucan	about 1-15 w/w %
triethanolamine	about 2 w/w %
sodium lauryl sulfate	about 1 w/w %
parabens	about 0.4 w/w %
suspending/viscosity increasing agent	about 0.1-8.0 w/w %
solvent	balance

wherein said solvent comprises about 50-70 w/w percent water and about 0-20 w/w percent oil of said composition; and

wherein said suspending/viscosity increasing agent includes at least one of polyvinyl alcohol and xanthan gum.

22. The topical composition of claim 1, wherein said composition is a cream, said composition comprising:

cereal-derived β-D-glucan at about 0.5-15w/w percent;

a solvent includingwaterataboutatleast50w/w percent of the composition;

a humectant;

a stiffening agent;

an emulsifying/solubilizing agent;

a suspending/viscosity increasing agent;

an antimicrobial agent; and

a plasticizer.

23. The topical composition of claim 1, wherein said composition is a gel having a gel base including water and at least one suspending/viscosity increasing agent.

24. The topical composition of claim 1, wherein said composition is a gel having a water base including at least about 80 w/w percent water.

25. The topical composition of claim 23, wherein said topical composition includes:
water about 80-98 w/w percent
suspending/viscosity increasing agent(s)
about 0.5-8.0 w/w percent.

26. The topical composition of claim 25, wherein said suspending/viscosity increasing agent(s) comprises at least one of a group including polyvinyl alcohol, carboxymethylcellulose and xanthan gum.

27. The topical composition of claim 25, wherein said suspending/viscosity increasing agents comprise polyvinyl alcohol plus one other.

28. The topical composition of claim 25, further comprising triethanolamine at about 0.1-5.0 w/w %.

29. The topical composition of claim 25, further comprising a chelating agent at about 0.01-1.0 w/w %.

30. The topical composition of claim 25, further comprising an antimicrobial agent.

31. The topical composition of claim 27, wherein said one other suspending/viscosity increasing agent comprises one of xanthan gum, agarose, alginate, guar gum, carboxymethylcellulose, and Carbopol™ 940 carbomer.

32. A composition of a multi-purpose topical gel, comprising:

water	about 80-98 w/w %
cereal-derived β-D-glucan	about 0.5-15 w/w %
triethanolamine	about 0.1-5.0 w/w %
carboxymethylcellulose	about 0.01-2.0 w/w %
polyvinyl alcohol	about 0.5-4 w/w %
carbomer	about 0.01-2.0 w/w %
EDTA	about 0.01-1.0 w/w %
paraben(s)	about 0.1-2.0 w/w %

33. The composition of claim 34, wherein said cereal-derived β-D-glucan is derived from one of oats and barley.

34. The composition of claim 32, wherein said cereal-derived β-D-glucan is characterized as (1-3)(1-4) β-D-glucan.

35. The composition of claim 32, wherein said cereal-derived β-D-glucan is characterized as having a number of (1-4) glucopyranosyl linkages equal to about 1.5 to 3.0 times the number of (1-3) glucopyranosyl linkages.

36. A composition of a multi-purpose topical gel, comprising:

water	about 92.9 w/w %
cereal-derived β-D-glucan	about 2.0 w/w %
triethanolamine	about 2.0 w/w %
carboxymethylcellulose	about 1.0 w/w %
polyvinyl alcohol	about 1.0 w/w %
Carbopol 940 carbomer	about 0.5 w/w %
EDTA	about 0.2 w/w %
methylparaben	about 0.2 w/w %
propylparaben	about 0.2 w/w %

37. The composition of claim 36, wherein said cereal-derived glucan is derived from oats.

38. The composition of claim 36, wherein said cereal-derived glucan is characterized as (1-3) (1-4) β-D-glucan.

39. A topical composition for burns, wounds, and scarring of the skin and mucosa, wherein said composition contains 0.5-15 w/w % cereal-derived β-D-glucan, said composition selectively formulated as one of the group comprising an unguent, cream, gel, emollient, oil and lotion.

AMENDED CLAIMS

[received by the International Bureau on 17 March 1999 (17.03.99);
new claims 40-47 added;
remaining claims unchanged (2 pages)]

38. The composition of claim 36. wherein said cereal-derived glucan is characterized as (1→ 3) (1→ 4) β-D-Glucan.

39. A topical composition for burns, wounds, and scarring of the skin and mucosa, wherein said composition contains 0.5-15 w/w % cereal-derived β-D-glucan, said composition selectively formulated as one of the group comprising an unguent, cream, gel, emollient, oil and lotion.

40. A method for treating burns and wounds and other skin loss injuries and conditions comprising the step of applying to the affected area of the skin of a patient a topical composition comprising cereal derived β-D-Glucan as an active ingredient.

41. The method of claim 40 wherein the topical composition comprises one of a cream base, a gel base and an oil base.

42. The method of claim 40 wherein the cereal derived β-D-Glucan is derived from one of barley, oats, and wheat.

43. A method for treating burns and wounds and other skin loss injuries and conditions comprising the step of applying to the affected area of the skin of a patient a topical composition comprising cereal derived β-D-Glucan characterized as (1→ 3) (1→ 4) β-D-Glucan as the active ingredient.

44. A method for treating burns and wounds and other skin loss injuries and conditions comprising the steps of:
cleansing thoroughly a wound area of damaged tissue;
applying to the wound a topical composition comprising a cereal derived β-D-Glucan as the active ingredient; and
repeating the application of the topical composition until healing is complete.

45. A method of treating burns and wounds and other skin loss injuries and conditions comprising the steps of:
cleansing thoroughly a wound area of damaged tissue;
applying a topical composition comprising a cereal derived β-D-Glucan characterized as (1→ 3) (1→ 4) β-D-Glucan as the active ingredient; and
applying repeatedly the topical composition until healing is complete.

46. A method for treating burns and wounds and other skin loss injuries and conditions comprising the steps of:
cleansing thoroughly a wound area of damaged tissue;
applying to the wound a topical composition comprising a cereal derived β-D-Glucan as the active ingredient; and
repeating the application of the topical composition.

47. A method of treating burns and wounds and other skin loss injuries and conditions comprising the steps of:
cleansing thoroughly a wound area of damaged tissue;
applying a topical composition comprising a cereal derived β-D-Glucan characterized as (1→ 3) (1→ 4) β-D-Glucan as the active ingredient; and,
repeating the application of the topical composition.

STATEMENT UNDER ARTICLE 19(1)

Claims 38 and 39 of replacement sheet 19 are unchanged from the original claims 38 and 39 filed on 20 October 1998. Claims 40 - 47 are new claims drawn to methods of treating burns and wounds and other skin loss injuries and conditions. These claims are based upon and enabled by the written specification of the above-named international application as it was filed on 20 October 1998.

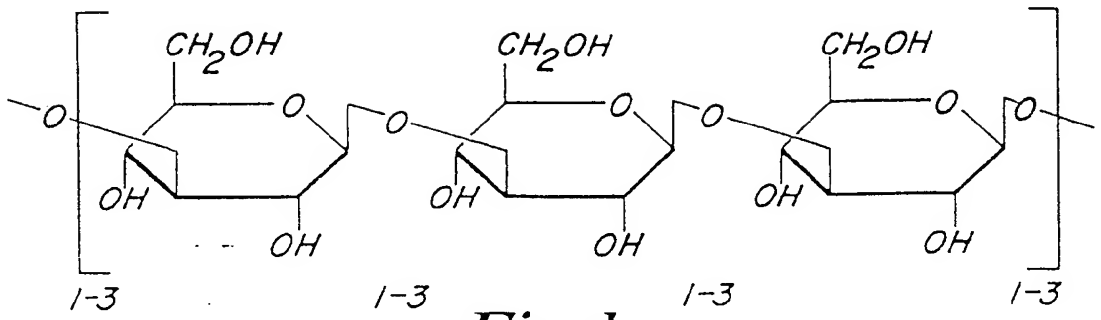

Fig 1

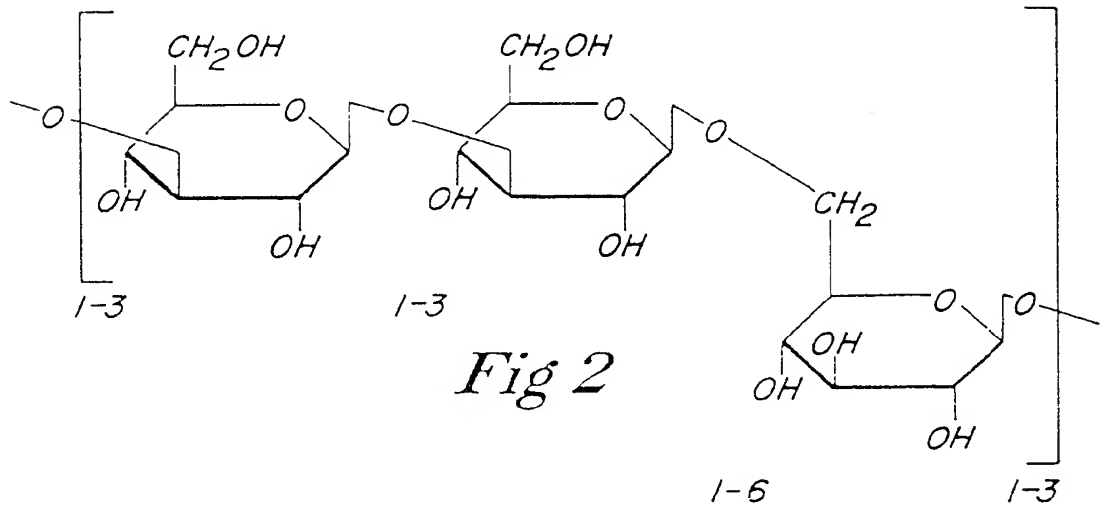

Fig 2

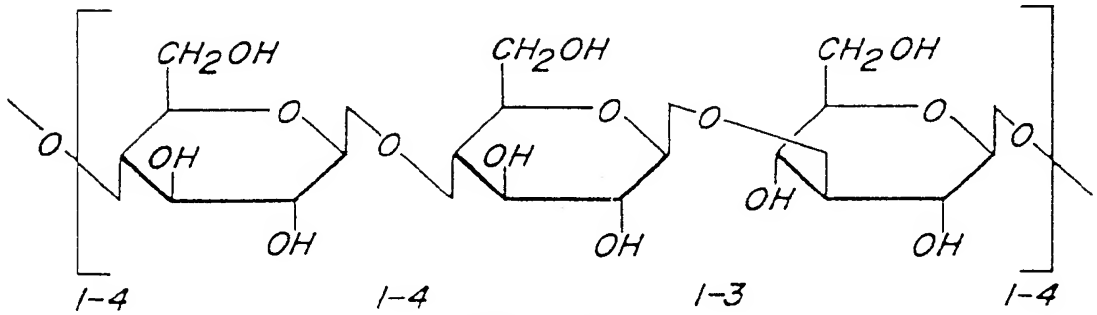

Fig 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/22108

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 7/48
US CL :424/401. 78.06, 78.07; 514/887
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/401. 78.06, 78.07; 514/887

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, BIOSIS, EMBASE, DERWENT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,658,957 A (MARTIN et al.) 19 August 1997, see col. 49, lines 35-55, col. 22, lines 67 - col. 23, line 3, col. 24, lines 4-31, col. 13, line 2, col. 47, lines 26-35, col. 51, line 63 and claim 17.	1-39
Y	Database BIOSIS on STN. TAMURA et al. 'Purification and characterization of a (2 fwdarw 3)-beta D-glucan binding protein from horseshoe crab (Tachyleus tridentatus) amoeboctyes)'. Carbohydrate Research. 1996, Vol. 295, pages 103-116 (English). Biological Abstracts Vol. 103 lss. 003 Ref. 039208.	1-39

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 29 JANUARY 1999	Date of mailing of the international search report 05 FEB 1999
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Form PCT/ISA/210 (second sheet)(July 1992)★